

(12) United States Patent

Vacanti et al.

4,228,243 A

4,239,664 A

4,243,775 A

(10) Patent No.:

US 6,348,069 B1

(45) Date of Patent:

Feb. 19, 2002

(54)	ENGINEERING OF STRONG, PLIABLE TISSUES				
(75)	Inventors:	Joseph P. Vacanti, Winchester; Christopher K. Breuer, Brighton; Beverly E. Chaignaud; Toshiraru Shin'oka, both of Brookline, all of MA (US)			
(73)	Assignee:	Children's Medical Center Corporation, Boston, MA (US)			
(*)	Notice:	Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.			
(21)	Appl. No.: 09/185,360				
(22)	Filed:	Nov. 3, 1998			
Related U.S. Application Data					
(62)	Division of application No. 08/445,280, filed on May 19, 1995, now Pat. No. 5,855,610.				
(51)	Int. Cl. ⁷ A61F 2/02				
(52)	U.S. Cl				
	Field of Search				
(56)	References Cited				
	U.S. PATENT DOCUMENTS				

4,277,582 A	7/1981	Mueller et al.
4,280,954 A		Yannas et al.
4,304,591 A	12/1981	Mueller et al.
4,304,866 A	12/1981	Green et al.
4,328,204 A	5/1982	Wasserman et al.
4,347,847 A	9/1982	Usher
4,348,329 A	9/1982	Chapman
4,352,883 A	10/1982	Lim
4,356,261 A	10/1982	Kuettner
4,391,797 A	7/1983	Folkman et al.
4,416,986 A	11/1983	Markus et al.
4,427,808 A	1/1984	Stol et al.
4,431,428 A	2/1984	Schmer
4,438,198 A	3/1984	Schmer
4,439,152 A	3/1984	Small
4,440,921 A	4/1984	Allcock et al.
4,444,887 A	4/1984	Hoffmann
4,446,229 A	5/1984	Indech
4,446,234 A	5/1984	Russo et al.
4,450,150 A	5/1984	Sidman
4,456,687 A	6/1984	Green
4,458,678 A	7/1984	Yannas et al.
4,485,096 A	11/1984	Bell
4,485,097 A	11/1984	Bell
4,489,056 A		Himmelstein et al.
4,494,385 A		Kuraoka et al.
4,495,174 A	1/1985	Allcock et al.
4,505,266 A		Yannas et al.
4,520,821 A	6/1985	Schmidt et al.
4,528,265 A		Becker
4,544,516 A		Hughes et al.
4,545,082 A		Hood
4,553,272 A	11/1985	Mears
(T	•	4 X

(List continued on next page.)

FOREIGN PATENT DOCUMENTS

AU	24245/88 B	2/1989	
DE.	28 53 614	7/1979	
DE	35 18 150	10/1986	
	(List continued on next page.)		
	OTHER PU	BLICATIONS	

Allcock & Kwon, "An Ionically Cross-Linkable Polyphosphazene: Poly[bis(carboxylatophenoxy)phosphazene] and Its Hydrogels and Membranes," *Macromolecules* 22:75–79

(1989).

(List continued on next page.)

Primary Examiner-David J Isabella (74) Attorney, Agent, or Firm-Holland & Knight LLP **ABSTRACT**

It has been discovered that improved yields of engineered tissue following implantation, and engineered tissue having enhanced mechanical strength and flexibility or pliability, can be obtained by implantation, preferably subcutaneously, of a fibrous polymeric matrix for a period of time sufficient to obtain ingrowth of fibrous tissue and/or blood vessels, which is the removed for subsequent implantation at the site where the implant is desired. The matrix is optionally seeded prior to the first implantation, after ingrowth of the fibrous tissue, or at the time of reimplantation. The time required for fibrous ingrowth typically ranges from days to weeks. The method is particularly useful in making valves and tubular structures, especially heart valves and blood vessels.

7 Claims, No Drawings

1,995,970 A	3/1935	Dorough
2,609,347 A	9/1952	Wilson
2,653,917 A	9/1953	Hammon
2,659,935 A	11/1953	Hammon
2,664,366 A	12/1953	Wilson
2,676,945 A	4/1954	Higgins
2,683,136 A		Higgins
2,703,316 A	3/1955	Schneider
2,758,987 A	8/1956	Salzberg
2,846,407 A	8/1958	Wilson
2,951,828 A	9/1960	Zeile et al.
3,514,791 A	• 6/1970	Sparks 623/66
3,531,561 A	9/1970	Trehu
3,826,241 A	7/1974	Bucalo
3,880,991 A	4/1975	Yolles
3,883,393 A	5/1975	Knazek et al.
3,902,497 A	9/1975	Casey
3,935,065 A	1/1976	Doerig
3,949,073 A	4/1976	Daniels et al.
3,960,150 A	6/1976	Hussain et al.
3,974,526 A	8/1976	Dardik et al.
3,992,725 A	11/1976	Homsy
3,995,444 A	12/1976	Clark et al.
4,026,304 A	5/1977	Levy
4,060,081 A	11/1977	Yannas et al.
4,069,307 A	1/1978	Higuchi et al.
4,137,921 A	2/1979	Okuzumi
4,141,087 A	2/1979	,
4,144,126 A	3/1979	Burbidge
4,186,448 A	2/1980	Brekke
4,192,827 A	3/1980	Mueller et al.
4,205,399 A	6/1980	Shalaby et al.

10/1980 Iizuka

12/1980 Teag et al.

1/1981 Rosensaft et al.